

**UNITED STATES DEPARTMENT OF COMMERCE****Patent and Trademark Office**

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/039,177	03/13/98	MIYAZONO	K LUD-5539

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HM12/1105

EXAMINER

FITZGERALD, D

ART UNIT	PAPER NUMBER
1646	10

DATE MAILED: 11/05/99

Please find below and/or attached an Office communication concerning this application or proceeding.

**Commissioner of Patents and Trademarks**

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/039,177	MIYAZONO ET AL.
Examiner	Art Unit	
David L. Fitzgerald	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE THREE MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

#### Status

- 1) Responsive to communication(s) filed on 18 August 1999.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 1-20, 25 and 27 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 21-24, 26 and 28 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claims 1-28 are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) All b) Some \* c) None of the CERTIFIED copies of the priority documents have been:
1. received.
2. received in Application No. (Series Code / Serial Number) 08/436,265-.
3. received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

#### Attachment(s)

- 14)  Notice of References Cited (PTO-892)                    17)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 15)  Notice of Draftsperson's Patent Drawing Review (PTO-948)                    18)  Notice of Informal Patent Application (PTO-152)
- 16)  Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_                    19)  Other: \_\_\_\_\_

1. Applicant's election without traverse of Group IV, claims 21-26 and 28 as they read on methods employing agents which promote Smad1 phosphorylation, in the reply filed 18 August 1999 (Paper No. 8) is acknowledged.

5 In response to the requirement for an election of species, applicant indicates election of molecules that bind to the extracellular domain of ALK-1. As a formal matter, this indication does not respond to the outstanding requirement because the subject matter which applicant has elected corresponds to a subgeneric claim limitation, not a species, *i.e.*, a single embodiment of the invention. Applicant further indicates, however, that claims 21-24, 26, and 28 read on the elected species. The only disclosed species on which the noted claims read is that recited in claim 10 23, *viz.*, a method using TGF- $\beta$ . Claim 24 requires "a portion of TGF- $\beta$  sufficient to bind to ALK-1," a subgenus which is related to the species of claim 23, *i.e.*, a method using the "intact" TGF- $\beta$ .

15 In view of the above, to permit acceptance of applicant's reply as responsive to the requirement for an election of species and to allow examination to proceed, the Office will construe applicant's reply as an election of the species of a method using TGF- $\beta$ . The Office will further withdraw the requirement for restriction as between the species of claim 23 (TGF- $\beta$ ) and the related subgenus of claim 24 (fragments of TGF- $\beta$ ).

Claims 1-20, 25, and 27 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b), as drawn to non-elected inventions.

20 2. Applicant did not respond to the examiner's request at ¶ 2 of Paper No. 7. Applicant is again requested to supply copies of any items which were submitted but are not now present in the application file.

25 Alternatively, if the items enumerated in the last Office letter are the only ones which were submitted on 02 October 1998, in order that the application fully comply with 37 C.F.R. §§ 1.821-1.825, applicant is required to submit a statement as to the identity of the computer-readable and paper-copy sequence listings and an amendment directing entry of the latter into the specification, including a statement to the effect that the amendment introduces no new matter.

30 3. The preliminary amendment filed concurrently with the application is objected to under 35 U.S.C. § 132 because it introduces new matter into the specification. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The

added material which is not supported by the original disclosure is the incorporation of the several U.S. and foreign priority applications, none of which formed a part of the instant specification as filed.

5       Applicant is required to cancel the new matter in the response to this Office action. Deletion of the last sentence in the amendatory material relating to incorporation by reference will obviate this ground of objection.

10      4.       The declaration is defective because it fails to identify the specification to which it is directed. The declaration identifies the application "filed on [blank] as Application Serial No. [blank];" furthermore, the attorney docket number at the top of the signature pages has been altered by hand, and the alteration is not initialed. A new oath or declaration in compliance with 37 C.F.R. § 1.67(a) identifying this application by its Serial Number and filing date is required. See M.P.E.P. §§ 602.01 and 602.02.

15      5.       The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20      The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

25      A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

30      With respect to application of the prior art, none of the applications to which priority is claimed under 35 U.S.C. §§ 119 and 120 describes the invention now claimed in the manner required by § 112, first paragraph. The claims are therefore not accorded benefit of any of the earlier filing dates.

35      6.       Claims 21-23 and 26 are rejected under 35 U.S.C. § 102(b) as being anticipated by either one of Yingling *et al.*, PNAS 93: 8940-44 (1996), or Lechleider *et al.*, JBC 271: 17617-20 (1996).

Each of the references describes the TGF- $\beta$ -induced phosphorylation of smad1 ( $\equiv$  bsp-1  $\equiv$  dwarfin-A; *see, e.g.*, Heldin *et al.*, *Nature* 390: 465-71 (1997) at 468, legend to Fig. 2) in a cellular system responsive to TGF- $\beta$ , and each teaches that the latter species participates in signaling pathways in response to TGF- $\beta$  (see the abstract of each; Yingling at 8941, col. 2, last paragraph; Lechleider at 17619, paragraph bridging columns). As was appreciated in the art at the time of the invention, signal transduction comprehends a series of molecular events by which the binding of a ligand at the surface of a cell indirectly induces modulation of transcriptional events in the nucleus of the cell, and indeed at the time of the invention several genes were known to be TGF- $\beta$ -responsive (see the introductions of the papers generally). The physiological response to TGF- $\beta$  described in the prior art therefore inherently involves "enhancing expression of a gene" as required by claim 21. TGF- $\beta$  is moreover inherently capable of binding to the extracellular domain of ALK-1 and of facilitating the interaction of the latter species and a type II receptor. The methods described in the prior art therefore expressly or inherently meet all of the limitations of the claims.

15 7. Claim 24 is rejected under 35 U.S.C. § 103(a) as being unpatentable over either one of Yingling, *PNAS* (1996), or Lechleider, *JBC* (1996).

Relevant disclosure of the references is discussed above in connection with the rejections under § 102. Neither describes the use of an active fragment of TGF- $\beta$ .

20 It would have been obvious to one having ordinary skill in the art at the time the invention was made to employ in the method of Yingling or Lechleider any fragment of TGF- $\beta$  known or reasonably expected to be capable of signaling in the same manner as native TGF- $\beta$ , *e.g.*, a species truncated by a small number of amino acid residues at the N- and/or C-termini, because the artisan would have expected to observe the same functional consequences as seen with native TGF- $\beta$  in the cellular systems described in the prior art. The claimed invention would have been 25 *prima facie* obvious as a whole at the time it was made, especially in the absence of evidence to the contrary.

8. Claim 28 is rejected under 35 U.S.C. § 103(a) as being unpatentable over either one of Yingling, *PNAS*, (1996) or Lechleider, *JBC* (1996) as taken in view of Basson *et al.*, *J. Cell. Physiol.* 153: 118-28 (1992).

Relevant disclosure of the Yingling and Lechleider references is discussed above in connection with the rejections under § 102. Neither describes the identification of transcripts corresponding to genes activated by TGF- $\beta$ .

5 Basson is relied on as it evidences that it was conventional in the art at the time of the invention to probe signaling pathways by isolating and identifying mRNA transcripts which are present at elevated levels in response to the signaling species, in this case TGF- $\beta$ 1 (see the abstract, Figs. 6 and 7, and the Discussion section generally).

10 It would have been obvious to one having ordinary skill in the art at the time the invention was made to identify transcripts whose expression is induced by TGF- $\beta$  in the NMuMg or L6 cells studied by Yingling or the A549 cells studied by Lechleider, using conventional methods (including unstimulated controls) such as those described by Basson, because the artisan would reasonably have expected that the mRNA transcripts so identified would correlate with TGF- $\beta$  signaling. It further would have been obvious to correlate elevated levels of the transcripts so identified with phosphorylation of smad1/bsp-1/Dwarfin-A because Yingling and Lechleider teach that such phosphorylation is involved in TGF- $\beta$ -mediated signaling. The claimed invention would have been *prima facie* obvious as a whole at the time it was made, especially in the absence of evidence to the contrary.

15

9. No claim is allowed.

10. Any inquiry concerning this communication should be directed to David Fitzgerald, who can be reached by any of the following means:

Telephone (703) 308-3934

Fax

All formal papers (703) 308-4242

Informal communications (703) 308-0294

e-mail (note PTO policies below) david.fitzgerald@uspto.gov

Inquiries of a general nature should be directed to the Technology Center 1 receptionists at (703) 308-0196.



DAVID L. FITZGERALD

PRIMARY EXAMINER

ART UNIT 1646

3 November 1999

The best time to reach **Examiner Fitzgerald** is from 9 a.m. to 4 p.m. (Eastern). If he cannot take a call, a message may be left on his voicemail. Should attempts to reach him be unsuccessful, the acting supervisor for this Art Unit, Paula Hutzell, may be reached at (703) 308-4310.

Most official papers and all informal communications may be submitted to the PTO by fax. For specific policies, refer to 37 C.F.R. § 1.6 and the notice published at 1096 O.G. 30. To facilitate their receipt and handling, please —

- ♦ Call the examiner when you send an urgent communication.
- ♦ **Do not send a duplicate copy by mail or courier.**

Any Internet e-mail communications will be made of record in the application file. PTO employees cannot engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. § 122. This policy is more fully set forth in the Interim Internet Usage Policy published in the PTO's *Official Gazette* on 25 February 1997 at 1195 O.G. 89.